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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
07/24/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/535,764	TSUCHIYA ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,9,12 and 15-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,9,12 and 15-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 4/24/2009 is acknowledged. Claims 3, 5-8, 10-11, 13, 14 are cancelled. Claims 27-30 are added.

Claims 1, 2, 4, 9, 12 and 15-30 are pending and examined on the merits.

Claim Rejections Withdrawn:

Claim Objections

The objection to claim 22 is withdrawn in view of the amendment to claim 22.

Claim Rejections – 35 USC § 112

The rejection of claims 15 and 16 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicants' persuasive arguments.

Claim Rejections – 35 USC § 102

The rejection of claims 1-4, 17, 20, 21 and 23 under 35 U.S.C. 102(b) as being anticipated by Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) as evidenced by Webster's New World™ Medical Dictionary (plasma cell. In Webster's New World™ Medical Dictionary, 2003. http://www.credoreference.com/entry/2438767) is withdrawn in view of the amendment to the claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-4, 14, 17-21 and 23 under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June) is withdrawn upon further consideration.

The rejection of claims 1-4, 9, 12, 17, 20, 21 and 23 under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Larrick (Immunological Reviews, 130: 1992; cited in the IDS) is withdrawn upon further consideration.

The rejection of claims 1-4, 9, 12, 14, 17-21 and 23 under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), and further in view of Larrick (Immunological Reviews, 130: 1992; cited in the IDS) is withdrawn upon further consideration.

The rejection of claims 1-4, 14, 17-23 and 25 under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001,

November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), and further in view of Koch (Koch, A. E. et al., American Journal of Pathology, 137 (5): 1199-1213, 1990) is withdrawn upon further consideration.

The rejection of claims 1-4, 14, 17-21, 23, 24 and 26 under 35 U.S.C. 103(a) as being unpatentable over Coronella (Coronella, J. A., Cancer Research, 61: 7889-7899, 2001, November 1) with evidentiary reference Webster's New World™ Medical Dictionary, in view of Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), and further in view of Mallison (Mallison, S. M. et al., Infection and Immunity, 59(11): 4019-4025, 1991) is withdrawn upon further consideration.

Claim Rejections Maintained and New Grounds of Rejection:

Claim Objections

Claims 18 and 19 are objected to for depending from canceled claim 3. Correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4, 15-21, 27 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June; of record) in view of Kotlan (Kotlan, B. et al., Immunology Letters, 65: 143-151, 1999; cited in IDS).

Obiakor teaches a method for isolating nucleic acid encoding an antibody wherein the method comprises isolating a single B cell from human or rabbit appendix tissue by the use of laser microdissection (LMD) and the use of PCR to obtain a polynucleotide encoding an antibody heavy chain and a polynucleotide encoding an antibody light chain of the isolated B

cell (page 56, right column; page 57, right column to page 58, left column). The method is repeated 8 times (see Table 4, page 60). The tissue is frozen, stained and fixed (dehydrated) (see Table 1, page 56).

Obiakor fails to teach the use of this method for isolating B cells and polynucleotides encoding an antibody from lesional tissue, such as cancer tissue.

However, the use of lesional tissue such as medullary breast cancer tissue as a source of tumor infiltrating B cells is known in the art as evidenced by the teachings of Kotlan. Kotlan teaches a method of isolating B-lymphocytes infiltrating a breast medullary carcinoma by generating a single suspension and amplifying VH, Vkappa, and Vlambda regions by RT-PCR (see abstract). The lesional tissue was obtained by surgical excision (see page 144, right column). The lesional tissue was frozen in liquid nitrogen (see page 144, right column). While Kotlan does not teach fixing of the lesional tissue, Obiakor teaches the use of fixed tissue use of LMD to isolate B cells. In either Obiakor or Kotlan the sequence of the variable region of the antibody heavy chain or light chain is obtained, and the both references teach a human B cell.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Obiakor for the purpose of obtaining polynucleotides encoding the VH, Vkappa or Vlambda regions from a B cell found in lesional tissue such as cancer tissue because Obiakor teaches the use of LMD and RT-PCR to determine the sequence of polynucleotides encoding antibodies from suspensions of single cells, where the cells are B cells. The rationale for combining the teachings of Obiakor with the teachings of Kotlan is that both Obiakor and Kotlan teach methods from the same field of endeavor, which is that of the isolation and determination of polynucleotide sequences of immunoglobulins from

single B cells. The difference between Obiakor and the instant claims is that Obiakor does not teach a lesional tissue, whereas the claims require a lesional tissue. However, because lesional tissues such as medullary breast cancer are known to contain B cells, and because there is reason to isolate and determine the polynucleotide sequences encoding antibodies in B cells infiltrating cancer tissues, and because Kotlan demonstrates that it is possible to isolate and determine the sequence of nucleotides encoding antibodies directed from B cells present in lesional tissue, the use of Obiakor's method with the lesional tissue of Kotlan appears to have a high probability of success.

Claims 9, 12, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June; of record) in view of Zhang (Zhang, H. et al., Cancer Research, 55: 3584-3591, 1995; cited in IDS).

The claims are drawn to method for producing an antibody wherein the method comprises isolating a single lesional tissue-infiltrating B cell from a lesional tissue by the use of LMD, obtaining a polynucleotide encoding an antibody heavy chain and a polynucleotide encoding an antibody light chain of the isolated B cell, preparing one or more expression vectors comprising the polynucleotides, transforming a host cell with the expression vectors, culturing the transformed host cell, and recovering the antibody expressed by the transformed host cell. Claim 12 adds the steps of contacting the antibody obtained by the method of claim 9 with a test lesional tissue, detecting binding between the antibody and the test lesional tissue and selecting the antibody if it binds to the test lesional tissue. The test lesional tissue may the lesional tissue

from which the B cells was isolated, or the test lesional tissue is from an individual different from the individual different from the individual from the whom the B cell was isolated.

Obiakor teaches a method for isolating nucleic acid encoding an antibody wherein the method comprises isolating a single B cell from human or rabbit appendix tissue by the use of laser microdissection (LMD) and the use of PCR to obtain a polynucleotide encoding an antibody heavy chain and a polynucleotide encoding an antibody light chain of the isolated B cell (page 56, right column; page 57, right column to page 58, left column). The method is repeated 8 times (see Table 4, page 60). The tissue is frozen, stained and fixed (dehydrated) (see Table 1, page 56).

Obiakor fails to teach the use of this method for isolating B cells and polynucleotides encoding an antibody from lesional tissue, such as cancer tissue. Obiakor fails to teach the additional steps of preparing expression vectors, transforming a host cells with the expression vectors, culturing the transformed host cell, and recovering the antibody expressed by the transformed host cell.

Zhang teaches a method of isolating polynucleotides encoding the variable regions of the heavy and light chains of antibodies produced by tumor-reactive B cells found in tumors (see page 3585). Zhang also teaches making antiserum from isolated B cells, as well as methods of making scFv antibodies in E. coli (page 3586). Zhang teaches method of testing the IgG supernatants from the B cells for binding to autologous as well as allogeneic tumors (page 3585, left column). The binding of scFv antibodies were tested against tumor cells lines (page 3585, left column).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Obiakor for the purpose of obtaining polynucleotides encoding antitumor antibodies from a B cell found in lesional tissue such as the melanoma tissue of Zhang, because Obiakor teaches the use of LMD and RT-PCR to determine the sequence of polynucleotides encoding antibodies from suspensions of single cells, where the cells are B cells, and because Zhang teaches that infiltrating B cells may be a source of anti-tumor antibodies (page 3585, left column). Zhang uses a different method for the isolation of tumor infiltrating B cells than that recited in the claims. However, as discussed above Obiakor provides evidence that the method of isolating a single B cell from a tissue using LMD is known in the art. Furthermore, because Zhang teaches that one goal of isolating infiltrating B cells from a tumor tissue is to detect anti-tumor antibodies and to use the polynucleotides encoding the anti-tumor antibodies in methods of making therapeutic anti-tumor antibodies, one would have been motivated to use the method of Obiakor as a method of isolating single B cells because the method of Obiakor ensures the detection of a single species of antibody in one isolation step. Thus, Zhang's method would be improved because Zhang's method requires more than one step to arrive a single monoclonal B cell population.

Claims 1, 2, 4, 15-23, 25 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), in view of Walton (Walton, L., J., et al., Atherosclerosis, 135: 65-71, 1997).

Obiakor teaches as set forth above.

Obiakor fails to teach the use of this method for isolating B cells and polynucleotides encoding an antibody from lesional tissue, such as an autoimmune disease lesion or an arteriosclerotic lesion.

However, the use of lesional tissue such as atherosclerotic abvcominal aortic aneurysms as a source of B cells for the detection of polynucleotides encoding antibodies is known in the art as evidenced by the teachings of Walton. Walton teaches a B cells are present in abdominal aortic aneurysm tissues (see Figure 1) and teaches a method of isolating DNA encoding immunoglobulin heavy chains to determine VH gene usage (page 67). Walton teaches that one desired aim in the art is to clone specific immunolgobline genes and subsequently identify the tissue antigens and their autoantigenic domains (see page 69, right column).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Obiakor for the purpose of obtaining polynucleotides encoding the polynucleotides encoding antibodies from a B cell found in lesional tissue such as an inflammatory atherosclerotic lesion, because Obiakor teaches the use of LMD and RT-PCR to determine the sequence of polynucleotides encoding antibodies from suspensions of single cells, where the cells are B cells to obtain monoclonal antibody species, and Walton teaches the desirability of isolating such antibodies for identification of tissue antigens. Furthermore, because Walton teaches that one goal isolating antibody-encoding polynucleotides from atherosclerotic lesions is to tissue autoantigens, one would have been motivated to use the method of Obiakor as a method of isolating single B cells because the method of Obiakor ensures the detection of a single species of antibody in one isolation step.

Claims 1, 2, 4, 15-21, 23-26 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Obiakor (Obiakor, H. et al., Analytical Biochemistry, 306: 55-62, 2002, June), in view of Mallison (Mallison, S. M. et al., Infection and Immunity, 59(11): 4019-4025, 1991).

Obiakor teaches as set forth above.

Obiakor fails to teach the use of this method for isolating B cells and polynucleotides encoding an antibody from lesional tissue, such as a lesion generated by an infectious pathogen or wherein the lesional tissue is an artificially prepared lesion.

The claims are drawn to methods for isolating nucleic acid encoding an antibody against lesional tissue, which is a method that results in identifying at least one antibody species, which is information that can be used to identify an antigen.

The methods of Obiakor may be used to study lesions such as those taught by Mallison. Mallison shows that in models of periodontal disease there is an influx of B cells in cases where there is chronic inflammation. Mallison teaches that more study is needed to understand the pathological process associated with periodontal disease (page 4024).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Obiakor to isolate single B cells and further to isolate and obtain polynucleotides encoding antibodies for the further understanding of pathological processes associated with periodontal disease. One would have had a reasonable expectation of success in using the method of Obiakor with the tissues of Mallison because Mallison demonstrates that B cells are present.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
July 20, 2009
/Alana M. Harris, Ph.D./
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